REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

I. EXAMINER INTERVIEW, CLAIM STATUS & AMENDMENTS

Claims 1-3 and 5-10 were pending in this application when last examined, and stand rejected.

Applicant thanks Examiners Salmon and Goldberg for the interview on April 13, 2006.

During the interview, Applicant proposed cancelling claims 1-7 and 10, and amending claim 8 to incorporate the subject matter of claim 1. The claims have been amended to effect these changes. Support for the amendment to claim 8 can be found in claim 1.

Claims 1-7 and 10 have been cancelled without prejudice or disclaimer thereto. Applicant reserves the right to file a divisional or continuation application on any cancelled subject matter.

New claims 11-16 have been added, which depend on claim 8. Support for the new claims can be found in original claims 2-7, respectively.

Therefore, no new matter has been added by this amendment.

Claims 8, 9 and 11-16 are pending upon entry of this amendment.

During the interview, it was agreed that the cancellation of claims 1-7 and 10 removes the 102(b) anticipation rejection over Livak (PCR Methods and Applications, Vol. 4, pp. 357-362, 1995). It was also indicated the Examiners would have to further consider whether the present amendment and arguments are sufficient to overcome the 103 rejection over Livak and the 112, first paragraph, enablement rejection.

II. PRIOR ART REJECTIONS

In item 1 on pages 3-4 of the Action, claims 1-3 and 7-9 were rejected under 35 U.S.C. § 102(b) as anticipated by Livak (PCR Methods and Applications, Vol. 4, pp. 357-362, 1995).

In item 2 on pages 4-6, claims 5, 6 and 10 were rejected under 35 U.S.C. § 103(a) as obvious over Livak (PCR Methods and Application, Vol. 4, pp. 357-362, 1995) in view of Livak (U.S. 5,723,591).

These rejections are respectfully traversed as applied to the amended and new claims.

To anticipate a claim, a cited prior art reference must teach each and every element of the claimed invention. See M.P.E.P. § 2131.01.

To establish obvious, three criteria must be met. First, the prior art references must teach or suggest each and every element of the claimed invention. See M.P.E.P. § 2143.03. Second, there must be some suggestion or motivation in the references to either modify or combine the reference teachings to arrive at the claim invention. See M.P.E.P. § 2143.01. Third, the prior art must provide a reasonable expectation of success. See M.P.E.P. § 2143.02.

As noted above, product claims 1-7 and 10 have been cancelled. During the interview, it was agreed that the cancellation of claims 1-7 and 10 should be sufficient to overcome the 102(b) rejection over Livak (1995).

Amended claim 8 is directed to a method for detecting a nucleic acid comprising contacting a probe with a nucleic acid sample, wherein the probe comprises a nucleic acid and further comprises a labeling substance that releases energy and an energy-absorbing substance that absorbs the energy released from the labeling substance, wherein the labeling substance is positioned on the nucleic acid 0 to 1 nucleotides apart from the energy-absorbing substance, and when the probe hybridizes with a target nucleic acid in the nucleic acid sample to form a hybridized double-stranded nucleic acid, the energy-absorbing substance interacts with the double-stranded nucleic acid and no longer absorbs the energy released from the labeling substance, thereby resulting in no quenching of the labeling substance, and measuring the energy related from the labeling substance.

Livak (1995) nowhere discloses a probe having a labeling substance that is 0 to 1 base pairs apart from the energy-absorbing substance that hybridizes with a target nucleic acid, thereby resulting in no quenching of the labeling substance. In other words, Livak (1995), fails

to disclose or suggest the method of the amended claim. In fact, Livak (1995) teaches away from the present invention for the reasons discussed below.

Livak (US '591) fails to remedy the deficiencies of Livak (1995).

Amended claim 8 requires that "when the probe hybridizes with a target nucleic acid in the nucleic acid sample to form a hybridized double-stranded nucleic acid, the energy-absorbing substance interacts with the double-stranded nucleic acid and no longer absorbs the energy released from the labeling substance thereby resulting in no quenching of the labeling substance." It is respectfully submitted that such language requires the sequential of steps of hybridization, interaction and no quenching by the enegy-absorbing substance. This language is consistent with the disclosure at page 8, lines 11-29.

Livak (US '591) simply fails to disclose or suggest this element of the claimed invention. In particular, Livak (US '591) fails to disclose the requirement for interaction to result in no quenching.

Also, the probe in Livak (US '591) is structurally different in that it involves a conformational change, not present in the claimed invention. The arguments set forth on pages 4-6 of the response filed February 4, 2005 with regard to Livak (US '591) are reiterated herein. In this regard, Livak (US '591) fails to teach a probe having "the labeling substance positioned on the nucleic acid 0 to 1 nucleotides apart from the energy-absorbing substance."

Instead, Livak (US '591) teaches (column 4, lines 41-45) that the "oligonucleotide probe also exists in at least one conformation when hybridized to a target polynucleotide where the quencher molecule is not positioned close enough to the reporter molecule to quench the fluorescence of the reporter molecule." (Emphasis added). Moreover, Livak (US '591) requires the reporter molecule to be separated from the quencher molecule by at least about 15 nucleotides. See Livak (US '591), column 5, lines 3-8. Accordingly, the probe in Livak (US '591) is structurally different from that of the claimed invention, and, in fact, Livak (US '591) teaches away from the claimed probe.

Therefore, Livak (US '591) fails to disclose or suggest, and in fact, teaches away from a probe having a labeling substance which is 0 to 1 nucleotide apart from the energy-absorbing substance.

Given this teaching way, Applicant respectfully submits that the prior art references lack motivation to combine their teachings to arrive at the claimed invention. It is well established that the prior art must be considered in its entirety and that the references cannot be combined where a reference teaches away from their combination. See M.P.E.P. § 2145, X, D, 2. Thus, it is respectfully submitted that Livak (US '591) cannot be combined with Livak (1995) to produce the probe in the claimed method.

Furthermore, it is respectfully submitted that the prior art references lack a reasonable expectation of success to arrive at the claimed invention. Upon reading Livak (US '591), one of ordinary skill in th art would not reasonably expect the probe to work when the reporter molecule is separated from the quencher molecule by less than 15 nucleotides. For this reason, the references lack a reasonable expectation of success of a probe having a labeling substance which is 0 to 1 nucleotide apart from the energy-absorbing substance in the claimed method.

In view of the above, the 102(b) rejection over Livak (1995) and the 103 obviousness rejection over Livak (1995) and Livak (US '591) are untenable and should be withdrawn.

III. ENABLEMENT REJECTION

In item 3 on pages 6-9 of the Action, claims 1-3 and 5-10 were newly rejected under 35 U.S.C. § 112, first paragraph, on the basis that the specification lacks enablement for the claimed invention. The Examiner was concerned with the limitation "wherein the labeling substance is positioned on the nucleic acid 0 to 1 nucleotides apart from the energy-absorbing substance." On page 7 of the Action, it was indicated that the specification does not enable the ability of the two dyes to function in such close proximity to one another. The Examiner also indicated that the specification does not teach how the non-quenching occurs with the two labels so close to one

another. On page 9 of the Action, it was indicated that the specification fails to provide a working example and/or data showing the successful use of such probes.

This rejection is respectfully traversed as applied to the amended claims and new claims.

The test of enablement is whether one reasonably skilled in the art can make or use the invention based on the disclosure in the specification coupled with the knowledge in the art without undue experimentation. See M.P.E.P. § 2164.01.

As noted during the interview, it appears that the previous Examiner misunderstood how the present invention works. Specifically, the Examiner assumed that the probe was cleaved between the labeling substance and the energy-absorbing substance. See page 7, lines 9-12 of the last Office Action. However, no cleavage is required in the instant invention. Instead, the energy-absorbing substance in the claimed probes specifically interacts with the double-stranded nucleic acid due to the hybridization of the probe with a target nucleic acid, thereby resulting in no quenching of the labeling substance. In other words, normally, the labeling substance releases energy and the energy absorbing substance absorbs this energy from the labeling substance. However, when the nucleic acid hybridizes with the target DNA, the energy transfer between the labeling substance and the energy-absorbing substance stops (*i.e.*, no quenching occurs). The detection mechanism of the present invention involves a fundamentally different process that does not involve a cleavage step as assumed by the Office. Thus, the claimed invention is completely different from that which is stated in the Office Action.

Furthermore, as discussed in the interview, Applicant respectfully submits that there is support for the claimed probe having the labeling substance positioned on the nucleic acid 0 to 1 nucleotides apart from the energy-absorbing substance. For instance, Example 1 at page 12, lines 20-30 is an example of a probe wherein the energy-absorbing substance (pyrene) is 0 nucleotides apart from the labeling substance. See the probe designated EFN1-FP at line 27 on page 12 of the specification. See also line 28 at page 12, probe EFN2-FP, which is a probe where the absorbing substance is 1 nucleotide apart from the labeling substance.

Furthermore, the present invention is supported by Nos. 14, 17, 21 and 24 in Table 1 on page 13.

Nos. 1 to 12 in Table 1 correspond to a probe having only the labeling substance, while Nos. 13 to 24 in Table 1 correspond to a probe having the labeling substance and the energy-absorbing substance.

Nos. 1 to 6 and 13 to 18 correspond to a probe targeted for the polynucleotide EC1, while Nos. 7 to 12 and 19 and 24 correspond to a probe targeted for the polynucleotide EC2.

Nos. 1 to 3, 7 to 9, 13 to 15, and 19 to 21 correspond to a probe, wherein the labeling substance is located 0 nucleotides apart from the energy-absorbing substance. Nos. 4 to 6, 10 to 12, 16 to 18, and 22 to 24 correspond to a probe, wherein the labeling substance is located 1 nucleotide apart from the energy absorbing substance.

Nos. 14, 17, 21, and 24 correspond to cases where both the labeling substance and the energy-absorbing substance are linked to probes and where their homologous sequences are provided in the solutions.

The chemical structures of the modified parts in Nos. 14 and 17 are shown in Figure 3.

As discussed on page 14, lines 15-22, the probes as shown in numbers 14, 17, 21 and 24 show an increase of fluorescent intensity upon hybridization. Accordingly, it is respectfully submitted that this disclosure amounts to working examples of the probe of the amended claims.

Based on these examples and the guidance in the disclosure, one of skill in the art could make and use the claimed probes without undue experimentation.

Therefore, the 112, first paragraph, enablement rejection is untenable and should be withdrawn.

CONCLUSION

In view of the foregoing amendments and remarks, it is respectfully submitted that the present application is in condition for allowance and early notice to that effect is hereby requested.

If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned attorney at the telephone number below.

Respectfully submitted,

Akio YAMANE

By: _____

Jay F. Williams
Registration No. 48,036
for
Warren M. Cheek, Jr.
Registration No. 33,367
Attorneys for Applicant

WMC/JFW/akl
Washington, D.C. 20006-1021
Telephone (202) 721-8200
Facsimile (202) 721-8250
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